Rabies — the Pirbright connection

J. CRICK*

Summary: In Great Britain, which is rabies-free, the use of veterinary vaccines is restricted to imported dogs and cats while in quarantine kennels and to animals of the same species destined for export. However, in most other countries where rabies is endemic there is a considerable demand for rabies vaccines for both human and animal use. For many years the Pirbright Institute has been engaged in developing methods for improving the efficacy of the veterinary vaccines.

One problem is antigenic variation among strains of virus selected for vaccine production and possible differences between these and field strains. In evaluating these differences, monoclonal antibodies are proving useful and, in this connection, at the Central Veterinary Laboratory, Weybridge, we are establishing a battery of hybridomas and a library of currently circulating strains of rabies and rabies-related virus strains. The importance of this work is shown by the identification since 1968 by ourselves and others of strains of Duvenhage virus near various ports in north-western Europe.

To control rabies in wildlife, workers in Switzerland and the Federal Republic of Germany have completed field vaccination trials using bait for foxes which contained attenuated virus. By this means the spread of the disease has been halted. However, there are inherent dangers in the use of live virus for this purpose and we have conducted experiments with laboratory animals using vaccines containing inactivated virus. We have also examined the possibility of any isolated virus glycoprotein (G) for general use in rabies vaccines. Biotechnology should permit the resolution of some of these problems encountered in the large-scale production and application of this type of vaccine.


Rabies is unlike any of the other diseases discussed at this meeting because, as far as is known, it infects all warm-blooded animals, including man. With certain exceptions — for example, cattle in Central and South America infected by vampire bat rabies; in Europe, the USSR and North America by fox rabies; and in southern Africa by rabid jackals — it is not a major problem among food animals. It does not therefore have a tremendous direct economic effect on the farming industry. Yet the cost of its prevention and control to the community at large is enormous and close cooperation between veterinary and medical authorities is required.

A WORLD CHALLENGE

Urban rabies, which involves domestic and feral dogs and cats, has been virtually eliminated from Europe apart from the south-eastern Mediterranean region,
but fox rabies has been spreading westward from the area of the present Polish/Russian border for the last forty years, reaching France in 1968. This movement of the disease is viewed with not a little anxiety by the Ministry of Agriculture, Fisheries and Food, whose veterinary service has the main responsibility for keeping rabies out of Britain. The prospect of a Channel tunnel and the recent identification of infected bats in Denmark are also a cause of some concern. Rapid and extensive international travel and massive trade links, particularly with the developing countries where the main rabies problems reside, also increase the opportunities for the introduction of infection and the possibility that British nationals may become infected while overseas.

Pirbright’s links with rabies may be said to have begun in 1936, when Dr Ian A. Galloway, its director from 1939 to 1963, attempted at the National Institute of Medical Research, Hampstead, with Dr W. J. Elford, to measure the size of the rabies virus particle, using ultrafiltration methods (14). It was more than thirty years later that work at AVRI on vesicular stomatitis virus (VSV), the prototype rhabdovirus, led Fred Brown and me to extend our experiments to rabies.

In Britain, the vaccination of animals against rabies is confined to imported cats and dogs (one dose on arrival in the quarantine kennels and a second four weeks later) or to animals to be exported (17). Since the days of Pasteur, vaccination has played an important part in the prevention of the disease, yet the enormity of the problem today can be judged from a recent estimate (1985) by the WHO that 850,000,000 animals and 5,600,000 humans throughout the world should be vaccinated each year if it is to be controlled. Consequently, a major part of our attention has been given to the development of better vaccines, improvement in methods of measuring vaccine potency and the consideration of antigenic variation between virus strains.

**EVALUATION OF VACCINE POTENCY**

Despite the fact that rabies virus is essentially neurotropic, it can be grown in a wide variety of cells in tissue culture. For the purpose of developing veterinary vaccines we restricted our work to the use of BHK 21 cells in both monolayers and suspended culture, using the Flury LEP and HEP 675 strains of virus. Both strains can be grown to titres of $10^7-10^8$ suckling mouse ID$_{50}$/ml and, after inactivation with AEI or BPL, will immunise animals effectively against the disease. These vaccines are now produced commercially and the 675 product is licensed for use in the UK for animals held in quarantine.

Probably because of its mode of transmission, rabies virus has fortunately never been responsible for major epidemics such as those caused by foot-and-mouth disease virus or influenza virus. Hence it is much more difficult to assess the efficacy of rabies vaccines in disease prevention. The only animals available in sufficient numbers for quality control are mice or guinea pigs; in cost alone, the routine vaccination and challenge of statistically significant numbers of dogs and cats for this purpose would be prohibitive. However, in the tests recommended by the WHO in 1973 for inactivated vaccines, the animals were given either 6 doses (Habel test) or 2 doses (NIH test) of vaccine before intracerebral challenge with standard virus (15). As an alternative, we suggested that serum neutralising antibody levels 14-21 days after a single dose of vaccine would provide a measure of vaccine
potency, i.e. protection against infection. We also showed that after more than one
dose of vaccine the boost in antibody production and hence great protection against
challenge could give a false assessment of the antigen concentration in the product
(7, 8, Table I). These results led in part to a decision to set up a collaborative study
in 1981 between 10 laboratories, including the Central Veterinary Laboratory
(CVL) at Weybridge, in which one- and two-dose NIH tests were compared. As a
result of these trials, a modified NIH test in which a single dose of vaccine is used
has now been adopted for the standardisation of veterinary vaccines for Europe
(see European Veterinary Pharmacopoeia).

<table>
<thead>
<tr>
<th>Vaccine dilution</th>
<th>Protected mice</th>
<th>SNA</th>
<th>Protected mice</th>
<th>SNA</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>20/20(a)</td>
<td>4.2(b)</td>
<td>14/20</td>
<td>3.4</td>
</tr>
<tr>
<td>50</td>
<td>13/20</td>
<td>3.7</td>
<td>8/20</td>
<td>2.7</td>
</tr>
<tr>
<td>250</td>
<td>4/18</td>
<td>2.3</td>
<td>4/19</td>
<td>1.1</td>
</tr>
<tr>
<td>1250</td>
<td>1/20</td>
<td>1.6</td>
<td>1/20</td>
<td>0.9</td>
</tr>
</tbody>
</table>

Inoculation

Day 0 and day 7

Day 0

(a) Mice challenged with 50 ID\(_{50}\) CVS 14 days after first dose of vaccine. 19/20 mice died in control group.
(b) Depression of virus titre (log\(_{10}\)) by 0.015 ml 1/10 pooled sera from groups of 4 mice 14 days after first dose of vac­
cine. Sera tested in suckling mice against CVS.

Nevertheless, it is obviously desirable to be able to monitor vaccine potency
with a suitable in vitro method. We have established a serum blocking test, using
aliquots of a standard hyperimmune rabies antiserum mixed with dilutions of vac­
cine, followed by a back titration of the remaining virus neutralising activity. For
this we use the rapid fluorescent focus inhibition test (RFFIT) developed at the
Communicable Diseases Center, Atlanta (15). A very simple modification of the
technique has been developed at Weybridge and is in routine use there (King and
Crick, manuscript in preparation).

**MONOCLONAL ANTIBODIES FOR THE CHOICE
OF VACCINE STRAINS**

We have always been concerned about antigenic variation between rabies strains
because we consistently found that, in neutralisation tests, homologous antibody
titres were always higher than heterologous titres. We have also found in NIH tests
(both with conventional 2-dose or the recently adopted 1-dose test) that protection
is greater against homologous strains than heterologous strains (9, Table II). These
findings raised the question whether the strains of virus used for vaccine production
and potency testing were the most suitable. How much did they differ from each
other and from currently circulating field strains? — questions vital to manufactu­
ners and public health authorities (9). With the development of monoclonal antibo­
dies and the advent of cloning and sequencing techniques, some of the answers are
being provided. In collaboration with our colleagues at the CVL, we are able to
TABLE II
Serum neutralising activity and protection of mice against intracerebral challenge
with either LEP or CVS virus after a single intraperitoneal dose of LEP vaccine

<table>
<thead>
<tr>
<th>Vaccine dilution</th>
<th>Protected mice</th>
<th>SNA</th>
<th>Protected mice</th>
<th>SNA</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>8/8a</td>
<td>4.5b</td>
<td>5/8</td>
<td>2.7</td>
</tr>
<tr>
<td>50</td>
<td>4/8</td>
<td>—</td>
<td>2/8</td>
<td>—</td>
</tr>
<tr>
<td>250</td>
<td>3/8</td>
<td>—</td>
<td>1/8</td>
<td>—</td>
</tr>
<tr>
<td>1250</td>
<td>1/8</td>
<td>—</td>
<td>0/8</td>
<td>—</td>
</tr>
<tr>
<td>Control (no vaccine)</td>
<td>1/8</td>
<td>—</td>
<td>0/8</td>
<td>—</td>
</tr>
</tbody>
</table>

Challenge virus
LEP CVS

(a) Mice challenged with either LEP or CVS virus (ca. 50 ID₅₀) 14 days after vaccination.
(b) Depression of virus titre (log₁₀) by 0.015 ml 1/10 pooled serum from a group of 8 mice 14 days after vaccination. Sera tested in suckling mice against LEP or CVS virus.

examine current street and laboratory strains of virus, using monoclonal antibodies provided by the Wistar Institute and CDC and also produced at Weybridge. From our own results (King and Crick, to be published) and those of other laboratories, patterns are emerging which indicate that it may be wise to produce polyvalent vaccines for use in certain regions. Importantly for Britain, we ought soon to be able to discern the origin of infection, should it occur.

INFECTION BY RABIES-RELATED VIRUSES

In 1972, after a meeting with other rhabdovirologists at Roscoff in France, we began working with the rabies-related viruses (13, 18). At that time Lagos bat virus had not been shown to produce clinical disease, even in bats, outside the laboratory. Mokola virus, despite isolations from two children in Nigeria with encephalitis, one of whom died, was regarded as a biological curiosity largely confined to shrews in West Africa. Since then, I have been told by several Nigerians of cases within their country of human encephalitis, some fatal, associated with shrews. There has also been a laboratory infection (L.G. Schneider, personal communication). Then, in 1982, Foggin reported a case of Mokola virus infection in a dog in Zimbabwe which had previously received a classical inactivated rabies vaccine; several cats were also infected (12). The outbreak occurred independently of classical rabies, which was also present in the same area. A Mokola type virus causing a rabies-like infection in a cat in Natal has also been described. This cat, like the dog in Zimbabwe, had also received a classical rabies vaccine (20).

On rare occasions between 1968 and 1985 isolates of Duvenhage virus have been found near ports in north-western Europe and it has been generally considered that the infected individuals had arrived in cargo by sea (19, 20). (Sick bats infected with Lagos bat, Mokola and Duvenhage virus have now been found in the Republic of South Africa) (16, 19, 20). In September 1985 a Danish school teacher was bitten by a bat which was also shown to be infected with Duvenhage virus and several more bats similarly infected have since been found over a wide area in Denmark (A.A.
King, personal communication). In collaboration with several other laboratories, we are examining at the CVL the European and South African bat isolates and the cat and dog isolates made by Foggin in Zimbabwe. In indirect fluorescent antibody tests using monoclonal antibody directed against nucleocapsid antigens, these viruses can be clearly differentiated from classical rabies virus strains but less obviously from each other or the prototype rabies-related viruses (A.A. King, personal communication). Perhaps more importantly, at the practical level, standard neutralisation tests indicate that protection from infection by any of them using currently manufactured vaccines could not be relied upon (Table III).

### Table III

Neutralisation of rabies and rabies-related virus strains
by human rabies immune globulin (HRIG)*

<table>
<thead>
<tr>
<th>Virus strain</th>
<th>Virus + PBS*</th>
<th>Virus + HRIG (1/50)*</th>
<th>Neutralisation index**</th>
</tr>
</thead>
<tbody>
<tr>
<td>CVS-11</td>
<td>4.3</td>
<td>0.5</td>
<td>3.8</td>
</tr>
<tr>
<td>58605 (French fox isolate)</td>
<td>3.5</td>
<td>≤0.5</td>
<td>≥3.0</td>
</tr>
<tr>
<td>Br 457/5 (Brazilian vampire bat isolate)</td>
<td>3.8</td>
<td>≤0.5</td>
<td>≥3.3</td>
</tr>
<tr>
<td>Lagos bat (prototype)</td>
<td>4.5</td>
<td>4.0</td>
<td>0.5</td>
</tr>
<tr>
<td>Mokola (prototype)</td>
<td>5.5</td>
<td>3.5</td>
<td>2.0</td>
</tr>
<tr>
<td>Mokola (dog, Zimbabwe)</td>
<td>4.9</td>
<td>2.8</td>
<td>2.0</td>
</tr>
<tr>
<td>Duvenhage (prototype)</td>
<td>5.5</td>
<td>3.5</td>
<td>2.0</td>
</tr>
<tr>
<td>SA 1486/2 (South African bat, Duvenhage)</td>
<td>4.5</td>
<td>2.3</td>
<td>2.2</td>
</tr>
<tr>
<td>Danish bat</td>
<td>3.8</td>
<td>1.3</td>
<td>2.5</td>
</tr>
</tbody>
</table>

* RFFIT (20). Virus titres expressed as log₁₀ TCID₅₀/50 µl. HRIG prepared from vaccinees who had received HDCV.

** Neutralisation index — depression of virus titre obtained by adding an equal volume of 1/50 HRIG to serial virus dilutions before the addition of suspended BHK 21 cells and incubation. After 48 hours the cells were fixed and stained with fluorescent-labelled rabies antiserum.

The recent Danish outbreak has emphasised the need for increased sophistication and precision within the UK for the identification of rabies and rabies-related viruses. To this end, the collection of strains initially begun at AVRI and transferred in 1979 to the CVL, when the Pirbright laboratory closed, is being extended. We are greatly helped in this by colleagues from both Pirbright and Weybridge on assignment abroad and by visitors to both laboratories who subsequently sent us material from their home countries. Increasing awareness of the importance of minimising the number of in vitro passage levels before examining field strains has led to the development of a rapid adaptation of the new isolates to BHK 21 cells. Essentially, the diagnostic material is homogenised and used to infect trypsinised cells, a portion of which are cultured separately from the bulk and stained with fluorescent antiserum after 24-48 hours incubation. At this time, usually, sufficient cells fluoresce for a diagnosis to be made and the remaining cultures are split before
further incubation. After 3-4 passages, 80-100% of cells usually fluoresce when the antiserum is added and there is sufficient virus in the supernatant fluid for further examination (A.A. King, unpublished data).

**VACCINATION TRIALS USING BAIT**

Because of the difficulties in controlling wildlife rabies, attempts are being made in North America and mainland Europe to develop oral vaccines which can be supplied to the vector species in bait. To date, modified live vaccines employed in carefully controlled trials in parts of Switzerland and the Federal Republic of Germany appear to have been successful in holding back the advance of the disease (21).

Similar trials are now proceeding in North America (D. Johnston, personal communication), and several other countries in Europe have expressed their intention of starting similar procedures. However, the deliberate dissemination of live virus, however innocuous the strain appears to non-target animals, is viewed with concern by many authorities including our own. Despite our rigorous precautions, it is still possible that rabies could become established within our very dense (and urbanised) fox population (10). In collaboration with workers from the University of North Wales in Bangor and, more recently, with the group in Ontario, we have been examining the feasibility of using a killed vaccine as an alternative to live virus in bait. So far, the materials have been given by mouth only to laboratory animals (guinea pigs and mice). On average, about 40-60% have shown sero-conversion, albeit at low levels, after one dose of vaccine and rather more after two doses (10, Table IV). However, the development in the USA of a vaccinia virus recombinant

<table>
<thead>
<tr>
<th>Vaccination protocol</th>
<th>SNA&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Vaccination protocol</th>
<th>SNA&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group A</strong></td>
<td></td>
<td><strong>Group B</strong></td>
<td></td>
</tr>
<tr>
<td>0.5 ml by mouth on day 0</td>
<td>6</td>
<td>0.5 ml by mouth on days 0 and 17</td>
<td>729</td>
</tr>
<tr>
<td></td>
<td>16</td>
<td></td>
<td>729</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td></td>
<td>27</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td></td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td></td>
<td>243</td>
</tr>
<tr>
<td><strong>Group C</strong></td>
<td></td>
<td><strong>Group D</strong></td>
<td></td>
</tr>
<tr>
<td>0.5 ml by mouth on day 0</td>
<td>16</td>
<td>0.5 ml by mouth on days 0 and 17</td>
<td>140</td>
</tr>
<tr>
<td>Fasted 24 hours before dose</td>
<td>6</td>
<td></td>
<td>140</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>Fasted 24 hours before each dose</td>
<td>46</td>
</tr>
<tr>
<td></td>
<td>81</td>
<td></td>
<td>729</td>
</tr>
<tr>
<td><strong>Group E</strong></td>
<td></td>
<td><strong>Group F</strong></td>
<td></td>
</tr>
<tr>
<td>0.5 ml i.p. on day 0</td>
<td>1263</td>
<td>No vaccine</td>
<td>53</td>
</tr>
<tr>
<td></td>
<td>243</td>
<td></td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>243</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>1263</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>1263</td>
<td></td>
<td>9</td>
</tr>
</tbody>
</table>

(a) SNA expressed as the reciprocal of the serum dilution at 50% endpoint measured against 10-30 TCID<sub>50</sub> homologous virus (HEP 675).
incorporating the rabies virus glycoprotein gene probably means that we should consider a change of tactics with regard to the loading of bait for the immunisation of wild animals (23). Success could mean extension of the method for the control of disease within uncontrolled dog and cat populations in countries where rabies is endemic.

SUB-UNIT VACCINES

Apart from the preceding reference, consideration of the glycoprotein (G), the spike protein on the virus particle, has been deferred until this point. However, our interest in structure/function relationships led us to consider the possibility of producing a rabies vaccine consisting solely of purified glycoprotein. Although Van den Ende et al. preceded us in recognising immunogenicity in rabies virus supernatants, they had concluded that this activity was due to residual whole virus particles rather than to virus sub-units (22). The experience gained at Pirbright by Brown and his collaborators with VSV led to the conclusion that in rabies virus, like VSV, a sub-unit (subsequently identified as the G protein) was the antigen responsible for the stimulation and production of neutralising antibody (1, 4, 5, Tables V and VI). However, isolated G protein proved too difficult to purify and maintain in a suitably antigenic form for large-scale vaccine production. Moreover, inoculation with virus G into guinea pigs and mice elicited a slower production of neutralising antibody than intact virion would do, an important consideration with regard to post-exposure therapy in man (1, Table VI). Biotechnology should enable this problem to be overcome and, in addition, permit the production of vaccines not necessarily more cheaply than in conventional tissue culture but certainly more safely.

### TABLE V

*Production of neutralising antibody in adult mice by inoculating fractions of inactivated rabies virus*

<table>
<thead>
<tr>
<th>Dilution of inoculum</th>
<th>Unfractionated virus (10^6.8)*</th>
<th>15,000 rev/min deposit (10^6.8)</th>
<th>Top 9 ml of supernatant (10^3.4)</th>
<th>Bottom 2 ml supernatant (10^3.2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/1</td>
<td>3.7</td>
<td>3.6</td>
<td>1.7</td>
<td>3.1</td>
</tr>
<tr>
<td>1/5</td>
<td>3.3</td>
<td>3.8</td>
<td>1.6</td>
<td>2.5</td>
</tr>
<tr>
<td>1/25</td>
<td>3.5</td>
<td>3.2</td>
<td>0.9</td>
<td>0.3</td>
</tr>
<tr>
<td>1/125</td>
<td>1.5</td>
<td>2.1</td>
<td>0.6</td>
<td>0.6</td>
</tr>
</tbody>
</table>

* ID<sub>50</sub>/ml
The figures in parentheses refer to the infectivity of the virus and fractions before inactivation with 0.05% acetylthylethelmine. The neutralising activity is the geometric mean of 4 sera in each group and is expressed as the depression of virus titre by 0.015 ml of 1/10 serum.

### TABLE VI

*Antibody response in guinea pigs to deoxycholate-treated inactivated rabies virus*

<table>
<thead>
<tr>
<th>Antigen</th>
<th>Log&lt;sub&gt;10&lt;/sub&gt; virus neutralised by 0.015 ml 1/20 antiserum*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>6 days</td>
</tr>
<tr>
<td>Virus</td>
<td>3.0</td>
</tr>
<tr>
<td>Virus + DOC</td>
<td>0.8</td>
</tr>
</tbody>
</table>

* Groups of 5 guinea pigs were vaccinated and bled by cardiac puncture. The figures given represent the average of the titres obtained from individual sera.
RABIES PATHOGENESIS

From the turn of the century until the 1960's very little progress was made in the understanding of rabies or rabies virus. Development of tissue culture techniques has subsequently allowed an extensive study of the virus in vitro, thereby establishing its position within the Rhabdoviridae. Consequently, in its overall strategy it is very much like VSV. Yet the tissue predilections of the two viruses in vivo are vastly different. Why?

It was exciting to find that rabies virus, like VSV and many other rhabdoviruses, produced shortened defective interfering (DI) particles (6). In the case of VSV, these have a massive effect on the production of infectious virions; with rabies virus the effect is much less marked and some strains seem scarcely to produce DI particles at all. It was tempting to speculate that the DI particles might have a role in the pathogenesis of rabies, in determining whether, in an animal, clinical signs would follow exposure to infection and, if so, how long the incubation period might be. However, workers at the Wistar Institute have been unable to correlate DI particle production with either attenuation or autointerference in mice (2) and their role, if any, in the disease process remains completely unknown.

OVERSEAS AID

It is impossible to conclude this article without referring to the role of Pirbright in relation to developing countries. We have had a number of overseas rabies virologists as visitors over the years and have gained from their experience in countries where rabies is endemic. In addition, the Institute played an important part in the Medical Research Council's clinical trial of the human diploid cell vaccine (HDCV) organised by the staff of the Clinical Research Centre at Harrow and initiated in August 1974. I would like to thank the 60 volunteers from within the Institute who took part in the trial. They willingly gave blood samples and, in some cases, whole units of blood which were used for the preparation in this country of the first batches of human rabies immune globulin (HRIG). Their cooperation was invaluable in ensuring the acceptance of HDCV and HRIG for use in Great Britain.

Sadly, after the smallpox incident in Birmingham in 1979, the AVRI rabies laboratory was no longer considered adequate for virus containment. Without the support, cooperation and patience of our colleagues, particularly Mr A.A. King, at the CVL, we should have been unable to continue our work over the last six years and we hope that the friendly collaboration will continue.

ACKNOWLEDGEMENT

I would particularly like to thank Mr A.A. King for permission to use previously unpublished results in Table III.

* *
LES ÉTUDES SUR LA RAGE A PIRBRIGHT. — J. Crick.

Résumé : En Grande-Bretagne, pays indemne de rage, l’emploi des vaccins vétérinaires est limité aux chiens et chats importés, pendant qu’ils sont maintenus dans les locaux de quarantaine, et aux animaux des mêmes espèces qui doivent être exportés. Cependant, dans la plupart des autres pays où la rage est endémique, les vaccins antirabiques, qu’ils soient destinés à l’homme ou aux animaux, font l’objet d’une demande considérable. Pendant des années, l’Institut de Pirbright a travaillé à mettre au point des méthodes en vue d’une meilleure efficacité des vaccins vétérinaires.

Un problème à résoudre est celui de la variation antigénique parmi les souches virales sélectionnées pour la production de vaccins et des différences éventuelles entre ces souches et les souches sauvages. Les anticorps monoclonaux se révèlent utiles pour évaluer ces différences et, dans ce contexte, notre équipe du Laboratoire Vétérinaire Central de Weybridge est en train de constituer un ensemble d’hybridomes et une banque des souches de virus rabique et de virus apparentés au virus rabique actuellement en circulation. L’identification depuis 1968, par notre équipe et par d’autres, de souches du virus Duvenhage près de différents ports du nord-ouest de l’Europe, montre l’importance de ce travail.

Pour combattre la rage sylvatique, les chercheurs de Suisse et de République Fédérale d’Allemagne ont réalisé des essais de vaccination sur le terrain au moyen d’appâts contenant du virus atténué. Cela a permis de stopper l’extension de la maladie. Toutefois, l’emploi de virus vivant à cette fin n’est pas sans danger et nous avons réalisé des expériences sur des animaux de laboratoire en utilisant des vaccins contenant du virus inactivé. Nous avons aussi étudié la possibilité de l’emploi généralisé de vaccins antirabiques à base de glycoprotéine virale isolée (G). La biotechnologie devrait permettre de résoudre certains des problèmes posés par la production et l’application à grande échelle de ce type de vaccin.


* * *

LOS ESTUDIOS DE LA RABIA EN PIRBRIGHT. — J. Crick.

Resumen : En Gran Bretaña, país libre de rabia, se limita el uso de las vacunas veterinarias a los perros y gatos importados, mientras están en los locales de cuarentena, y a los animales de estas mismas especies que deben ser exportados. Sin embargo, en la mayoría de los demás países en los que es endémica la rabia, es grande la demanda de vacunas antirrábicas para el hombre o para los animales. Durante años, el Instituto de Pirbright ha venido trabajando para elaborar métodos enfocados a la mejor eficacia de las vacunas veterinarias.

Un problema por resolver es el de la variación antigénica entre las cepas virales seleccionadas para la producción de vacunas y de las posibles diferencias entre las aludidas cepas y las cepas silvestres. Los anticuerpos monoclonales resultan de utilidad para evaluar estas diferencias y, en este contexto, nuestro equipo del Laboratorio Veterinario Central de Weybridge está constituyendo una unidad de hibridomas y un banco de cepas de virus rábico y de virus emparentados al virus rábico que circulan en la actualidad. La importancia de este trabajo queda evidenciada por la identificación desde 1968, por
nuestro equipo y por otros, de cepas del virus Duvenhage cerca de distintos puertos del Noroeste de Europa.

Para combatir la rabia selvática, los investigadores de Suiza y República Federal de Alemania efectuaron pruebas de vacunación de campo con cerdos que contenían virus atenuado, destinados a los zorros, con lo que se pudo detener la extensión de la enfermedad. Sin embargo, no deja de ser peligroso el uso de virus vivo para este fin, por lo que hemos efectuado experiencias con animales laboratoriales utilizando vacunas de virus inactivado. Hemos estudiado asimismo la posibilidad del empleo generalizado de vacunas antirrábicas a base de glicoproteína viral aislada (G). Con la biotecnología se deberán poder resolver algunos problemas que plantean la producción y aplicación a gran escala de este tipo de vacuna.


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REFERENCES


